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1-Year Clinical Outcomes of Diabetic Patients Treated With Everolimus-Eluting Bioresorbable Vascular Scaffolds

A Pooled Analysis of the ABSORB and the SPIRIT Trials

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Objectives The aim of this study was to evaluate 1-year clinical outcomes of diabetic patients treated with the Absorb bioresorbable vascular scaffold (BVS).

Background Clinical outcomes of diabetic patients after BVS implantation have been unreported.

Methods This study included 101 patients in the ABSORB Cohort B trial and the first consecutive 450 patients with 1 year of follow-up in the ABSORB EXTEND trial. A total of 136 diabetic patients were compared with 415 nondiabetic patients. In addition, 882 diabetic patients treated with everolimus-eluting metal stents (EES) in pooled data from the SPIRIT trials (SPIRIT FIRST [Clinical Trial of the Abbott Vascular XIENCE V Everolimus Eluting Coronary Stent System], SPIRIT II [A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System], SPIRIT III [Clinical Trial of the XIENCE V Everolimus Eluting Coronary Stent System (EECSS)], SPIRIT IV Clinical Trial [Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System]) were used for the comparison by applying propensity score matching. The primary endpoint was a device-oriented composite endpoint (DoCE), including cardiac death, target vessel myocardial infarction, and target lesion revascularization at 1-year follow-up.

Results The cumulative incidence of DoCE did not differ between diabetic and nondiabetic patients treated with the BVS (3.7% vs. 5.1%, $p = 0.64$). Diabetic patients treated with the BVS had a similar incidence of the DoCE compared with diabetic patients treated with EES in the matched study group (3.9% for the BVS vs. 6.4% for EES, $p = 0.38$). There were no differences in the incidence of definite or probable scaffold/stent thrombosis (0.7% for both diabetic and nondiabetic patients with the BVS; 1.0% for diabetic patients with the BVS vs. 1.7% for diabetic patients with EES in the matched study group).

Conclusions In the present analyses, diabetic patients treated with the BVS showed similar rates of DoCEs compared with nondiabetic patients treated with the BVS and diabetic patients treated with EES at 1-year follow-up. (ABSORB Clinical Investigation, Cohort B; NCT00856856; ABSORB EXTEND Clinical Investigation; NCT01023789; Clinical Trial of the Abbott Vascular XIENCE V Everolimus Eluting Coronary Stent System [SPIRIT FIRST]; NCT00180453; A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System [SPIRIT II]; NCT00180310; Clinical Trial of the XIENCE V Everolimus Eluting Coronary Stent System [EECSS] [SPIRIT III]; NCT00180479; Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System [SPIRIT IV Clinical Trial]; NCT00307047). (J Am Coll Cardiol Intv 2014;7:482–93) © 2014 by the American College of Cardiology Foundation

A dramatic increase in the incidence of diabetes mellitus has been recognized as a serious worldwide issue (1). Diabetes causes systemic microvascular and macrovascular complications including coronary artery disease (CAD) that ultimately contributes to cardiovascular mortality (2,3).

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Drug-eluting stents (DES) considerably reduce the need for repeat revascularization in diabetic patients compared with bare-metal stents (BMS) (4). The presence of diabetes, however, has still been associated with an increased risk of adverse clinical events after percutaneous coronary intervention (PCI) with DES (5,6). Although newer generation DES have generally shown better long-term outcomes compared with first-generation DES (7–9), a pooled analysis of 4 randomized trials using newer generation everolimus-eluting metal stents (EES) showed a marked attenuation of beneficial effects compared with first-generation paclitaxel-eluting stents in a subset of diabetic patients (10). The best type of DES for the treatment of diabetic patients remains unclear.

Bioresorbable vascular scaffolds (BVSs) are a novel approach to the treatment of CAD in that they provide transient vessel support and drug delivery to the vessel wall (11). The ABSORB Cohort B trial investigating the current generation of the everolimus-eluting BVS system (Absorb BVS, Abbott Vascular, Santa Clara, California) has shown an acceptable incidence rate of major adverse cardiac events (10.0%) without any scaffold thrombosis up to 3 years of follow-up (12).

To date, clinical outcomes of diabetic patients treated with the Absorb BVS have not been specifically described. Thus, the aim of this study was: 1) to assess the 1-year clinical outcomes of diabetic patients treated with the Absorb BVS compared with nondiabetic patients, using pooled individual data of the ABSORB Cohort B and the ABSORB EXTEND trials; and 2) to compare the 1-year clinical outcomes of diabetic patients treated with the Absorb BVS with that of diabetic patients treated with EES, using propensity-score (PS) matching of pooled data from the SPIRIT trials (SPIRIT FIRST [A Clinical Trial of the Abbott Vascular XIENCE V Everolimus Eluting Coronary Stent System], SPIRIT II [A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System], SPIRIT III [Clinical Trial of the XIENCE V Everolimus Eluting Coronary Stent System (EECSS)], SPIRIT IV Clinical Trial [Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System]).

Methods

Study population. We included all patients enrolled in the ABSORB Cohort B trial and the first consecutive 450 patients with 1 year of follow-up in the ABSORB EXTEND trial. As enrollment in the ABSORB EXTEND trial was completed on October 2, 2013, clinical follow-up is currently ongoing, and the data for this analysis were obtained from an interim data cutoff date of December 3, 2012. The details of these 2 trials have been described elsewhere (13,14). In brief, both trials were prospective, multicenter, single-arm studies assessing the safety and feasibility of the Absorb BVS. Patients older than 18 years of age who have 1 or 2 de novo lesions located in a different major epicardial vessel were enrolled. Target lesions must have a visually estimated stenosis of ≥50% and <100% and a Thrombolysis In Myocardial Infarction flow grade of ≥1. Major exclusion criteria were patients presenting with an acute myocardial infarction (MI), left ventricular ejection fraction <30%, renal insufficiency, aorto-ostial lesions, left main coronary artery lesions, total occlusions, heavily calcified lesions, and lesions with visible thrombus.

Abbreviations and Acronyms

ARC = Academic Research Consortium
BMS = bare-metal stent(s)
BVS = bioresorbable vascular scaffold
CAD = coronary artery disease
DES = drug-eluting stent(s)
DoCE = device-oriented composite endpoint
EES = everolimus-eluting metal stent(s)
MI = myocardial infarction
PCI = percutaneous coronary intervention
PoCE = patient-oriented composite endpoint
PS = propensity score
ST = scaffold/stent thrombosis
TLR = target lesion revascularization

For the current analysis, diabetic patients treated with the XIENCE V EES (Abbott Vascular) were pooled from the SPIRIT FIRST, the SPIRIT II, the SPIRIT III and the SPIRIT IV trials as

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historical controls. The details of all these SPIRIT trials were also described previously (7,8,15,16). Of note, major inclusion and exclusion criteria of these trials were similar to those of the ABSORB Cohort B and the ABSORB EXTEND trials, whereas inclusion criteria of the SPIRIT IV trial were more liberal than the other trials by permitting enrollment of patients with complex lesions that were defined as a maximum of 3 target lesions in 3 separate major epicardial coronary arteries, a maximum of 2 target lesions in a single coronary artery, an ostial right coronary artery lesion, or bifurcation lesions in which the side branch was ≥2 mm in diameter or the ostium of the side branch was >50% stenosed (8). The features of the aforementioned trials are summarized in Online Table 1.

All of these trials were sponsored and funded by Abbott Vascular. The research ethics committee of each participating institution approved the protocol, and all enrolled patients provided written informed consent before inclusion.

Study devices and treatment procedure. The details of study devices and diabetic treatment are presented in the Online Appendix. Lesions were treated using standard interventional techniques, with mandatory pre-dilation and scaffold/stent implantation at a pressure not exceeding the burst pressure rate. Post-dilation was left to the discretion of the operator and only permitted with balloons sized to fit within the boundaries of the scaffold/stent. Patients were treated with aspirin ≥80 mg pre-procedurally. A ≥300-mg loading dose of clopidogrel between 6 and 24 h before the procedure was required. After the index procedure, aspirin ≥75 or 80 mg daily throughout the duration of the trial and clopidogrel 75 mg daily for a minimum of 6 months should be administered except for the SPIRIT FIRST trial (a minimum of 3 months for clopidogrel).

Definition of clinical outcomes. In the present analysis, the primary clinical outcome was assessed by a device-oriented composite endpoint (DoCE), which is also known as target lesion failure at 1 year after the index procedure. This was defined as a composite of cardiac death, target vessel MI, or ischemia-driven target lesion revascularization (TLR). Secondary clinical outcome was a patient-oriented composite endpoint (PoCE) that was defined as a composite of all-cause death, all MIs, or any repeat revascularization. These classifications of outcome measures were on the basis of the Academic Research Consortium (ARC) definitions (17). In the event of a death that could not be attributed to another cause, it was considered as a cardiac death. The incidence of scaffold/stent thrombosis (ST) according to the ARC criteria is also reported up to 1 year of follow-up. Per-protocol MI was defined either as the development of new Q waves or as an increase in the creatine kinase level to greater than twice the upper limit of normal, accompanied by an increased level of creatine kinase-myocardial band (18). Notably, this definition of per-protocol MI was consistently applied in all trials used for the present analysis. All clinical outcomes were adjudicated by an independent clinical events committee.

Clinical follow-up and source document verification. Except for the studies with planned angiographic follow-up at 1 year, patients were clinically followed by their visits to the outpatient clinic or by telephone calls. In the ABSORB Cohort B, the SPIRIT FIRST, the SPIRIT II, the SPIRIT III, and the SPIRIT IV trials, source document verification was performed in 100% of patients through 1-year follow-up. In the ABSORB EXTEND trial, source document verification was routinely performed in 100% of patients through 30-day follow-up, subsequently in a random 20% of patients, and in 100% of all reported events for the remaining follow-up period.

Statistical analysis. For the present analyses, individual data were pooled on a patient-level basis. Continuous variables are expressed as mean ± SD and categorical variables are presented as proportion (%). Comparisons were performed by the *t* test for continuous variables and by chi-square or Fisher exact test when the Cochran rule is not met for categorical variables. Time-to-event variables are presented as Kaplan-Meier curves. Subjects were counted only once for a composite endpoint in hierarchical order, whereas the incidence of the components and ST events are shown in nonhierarchical order. PS matching was applied to compare 1-year clinical outcomes of diabetic patients treated with the BVS and those treated with EES. The details of PS matching are presented in the Online Appendix. Considering the larger number of diabetic patients treated with EES (N = 882) compared with that of diabetic patients treated with the BVS (N = 136), a 1:2 matching (BVS:EES) was performed in this study. A 2-sided p value <0.05 was considered statistically significant.

Results

Study population. A flow diagram of this study is shown in Figure 1. We included 101 patients in the ABSORB Cohort B trial and 450 patients in the ABSORB EXTEND trial. All patients were treated with the Absorb BVS and were classified as either diabetic (n = 136) or nondiabetic (n = 415). For diabetic patients treated with EES as a control group, we first excluded the patients with complex lesions in the SPIRIT IV trial (n = 128). In addition, 2 patients in the SPIRIT III trial and 26 patients in the SPIRIT IV trial were excluded because of the lack of 1-year follow-up data. A total of 882 diabetic patients treated with EES in a pooled study group from the SPIRIT trials was used for the comparisons between the BVS and EES.

Of these diabetic patients, the PS was not assessable for 11 of 136 patients in the BVS group and 221 of 882 patients in the EES group because of missing baseline characteristics

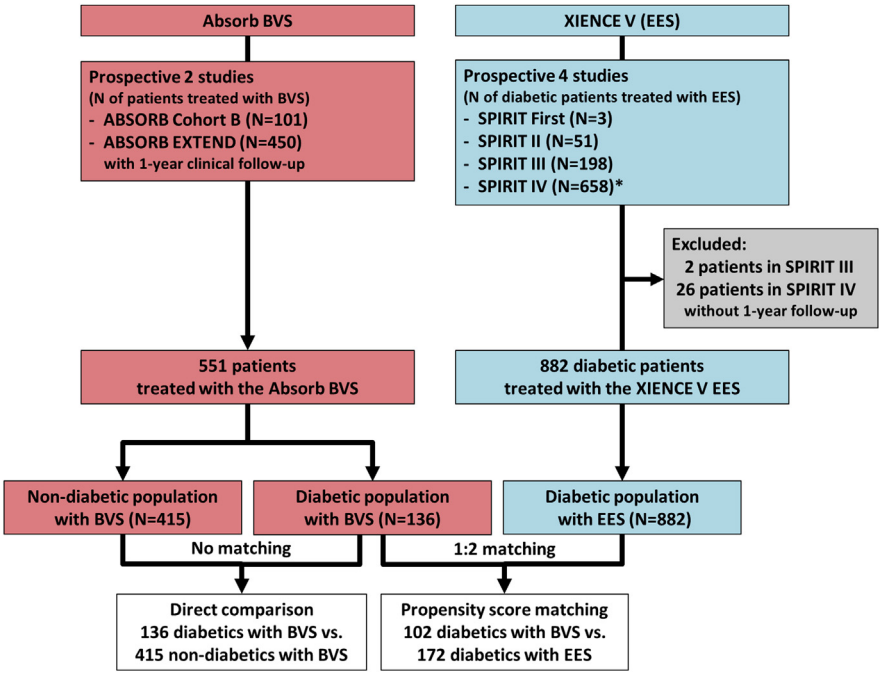

Figure 1. Flow Diagram of This Study

Asterisk indicates diabetic patients in the SPIRIT IV trial after excluding those with complex lesions, defined as triple-vessel treatment, ≥2 lesions per vessel treatment, lesions involving ostial right coronary artery lesions, or bifurcations lesions in which the side branch was ≥2 mm in diameter or the ostium of the side branch was >50% stenosed. BVS = bioresorbable vascular scaffold; EES = everolimus-eluting metal stent(s).

necessary to compute the PS. By applying the aforementioned methodology of PS matching, 23 patients in the BVS group and 489 patients in the EES group were excluded during the matching process. Consequently, there were 102 diabetic patients in the BVS group matched with 172 diabetic patients in the EES group for the comparative analyses.

Comparisons between diabetic and nondiabetic patients treated with the BVS. Patient demographics were comparable between diabetic and nondiabetic patients treated with the BVS, except for a history of hypertension requiring medication that was more prevalent in diabetic patients (Table 1). Lesion characteristics were also comparable between the 2 groups, except for the left anterior descending artery target lesion location being less prevalent in diabetic patients. Use of dual antiplatelet therapy did not differ between the 2 groups at each time point (at discharge, 6 months, and 1 year after the index procedure).

Time-to-event curves showing the cumulative incidence of DoCE and the components up to 1 year after the index procedure appear in Figure 2. DoCE at 1 year occurred in 3.7% of diabetic patients and 5.1% of nondiabetic patients ($p = 0.64$). There were no significant differences in the incidence of the components up to 1 year of follow-up between the 2 groups (Table 2). Similarly, PoCE was observed in 7.4% of diabetic patients and 8.2% of nondiabetic patients ($p = 0.86$). One patient with diabetes experienced definite late ST (0.7%), whereas 1 definite and 1 probable subacute ST and 1 definite late ST (0.7%) were observed in the nondiabetes group ($p = 1.0$).

Comparisons between the BVS and EES in diabetic patients. In the entire study groups with diabetes, the mean age, rates of hypertension requiring medication, hypercholesterolemia requiring medication, diabetes requiring insulin treatment, family history of CAD, previous coronary intervention, multivessel disease, type B2/C lesion, lesion length, reference vessel diameter, and percent of diameter stenosis were significantly greater in the EES group than in the BVS group. Conversely, male sex, rates of diabetes requiring oral hypoglycemic agents, unstable angina, and minimal luminal diameter were significantly less in the EES group (Table 3). After PS matching, all variables became comparable between the BVS group (102 patients) and the EES group (172 patients), except for left anterior descending artery target lesion location being less prevalent in the BVS group. Use of dual antiplatelet therapy was also comparable between the 2 treatment groups.

In the matched study group, DoCE at 1 year occurred in 3.9% of patients in the BVS group and in 6.4% of patients in the EES group ($p = 0.38$) (Fig. 3). There were no significant differences in the incidence of each component and

Table 1. Baseline Characteristics of Diabetic and Nondiabetic Patients Treated With the Absorb BVS

	Absorb BVS Diabetes (n = 136)	Absorb BVS Nondiabetes (n = 415)	p Value
Demographic characteristics			
Age, yrs	61.6 ± 10.0 (136)	61.9 ± 10.5 (415)	0.81
Male	73.5 (100/136)	73.7 (306/415)	1.00
Current smoker	19.9 (27/136)	21.0 (87/414)	0.81
Hypertension requiring medication	75.0 (102/136)	61.4 (254/414)	0.004
Hypercholesterolemia requiring medication	67.6 (92/136)	63.6 (264/415)	0.41
Diabetes treatment			
Insulin	16.9 (23/136)	0.0 (0/415)	<0.001
Oral hypoglycemic drugs	74.3 (101/136)	0.0 (0/415)	<0.001
Physical exercise and/or diet modification only	4.4 (6/136)	0.0 (0/415)	<0.001
No treatment	4.4 (6/136)	100.0 (415/415)	<0.001
Family history of coronary artery disease	41.4 (53/128)	37.2 (148/398)	0.40
Unstable angina	33.8 (46/136)	27.7 (115/415)	0.19
Previous coronary intervention	23.5 (32/136)	24.6 (102/415)	0.80
Previous myocardial infarction	26.5 (36/136)	28.8 (119/413)	0.66
Multivessel disease	23.5 (32/136)	17.6 (73/415)	0.13
Target vessel	144 lesions	439 lesions	
Right coronary artery	36.8 (53/144)	28.2 (124/439)	0.06
Left anterior descending artery	36.1 (52/144)	45.8 (201/439)	0.043
Left circumflex artery or ramus	27.1 (39/144)	26.0 (114/439)	0.83
Left main coronary artery	0.0 (0/144)	0.0 (0/439)	NA
ACC/AHA lesion class	143 lesions	434 lesions	
A/B1	62.9 (90/143)	59.7 (259/434)	0.49
B2/C	37.1 (53/143)	40.3 (175/434)	0.49
Target lesion characteristics	144 lesions	439 lesions	
Lesion length, mm	11.7 ± 5.1 (143)	11.2 ± 4.6 (429)	0.25
Pre-procedure			
Reference vessel diameter, mm	2.60 ± 0.33 (143)	2.62 ± 0.37 (429)	0.69
Minimal luminal diameter, mm	1.07 ± 0.33 (144)	1.08 ± 0.30 (434)	0.79
% Diameter stenosis	58.8 ± 10.8 (144)	58.4 ± 10.3 (433)	0.70
Dual antiplatelet therapy*	136 patients	415 patients	
At discharge	100.0 (136/136)	99.5 (413/415)	1.00
At 6 mo	96.3 (131/136)	97.1 (403/405)	0.58
At 1 yr	82.4 (112/136)	82.9 (344/415)	0.90

Values are mean ± SD (N) and % (n/N). *Patients taking both aspirin and thienopyridine.
NA = not available; ACC/AHA = American College of Cardiology/American Heart Association; BVS = bioresorbable vascular scaffold.

definite/probable ST at 1-year follow-up between the 2 treatment groups (Table 4). Similarly, PoCE was observed in 7.8% of the BVS group and in 11.0% of the EES group, where the difference was not statistically significant (p = 0.39).

Incidence of adverse events according to diabetes status in patients treated with the BVS. In the present analysis, the BVS cohort included 415 nondiabetic patients, and 113 noninsulin-treated and 23 insulin-treated patients with diabetes. The incidences of DoCE, PoCE, and their components at 1 year according to diabetes status are shown in Figure 4. Insulin-treated diabetic patients tended to have a higher rate of adverse events compared with nondiabetic and noninsulin-treated diabetic patients, whereas these differences did not reach statistical significance (5.1% in no diabetes, 2.7% in noninsulin-treated diabetes, and 8.7% in insulin-treated diabetes for DoCE [p = 0.37]; 8.2% in no diabetes, 7.1% in noninsulin-treated diabetes, and 8.7% in insulin-treated diabetes for PoCE [p = 0.92]).

Discussion

This is the first study addressing the clinical outcomes of diabetic patients treated with the Absorb BVS. The main findings of the present study can be summarized as follows: 1) there were no significant differences in 1-year rates of DoCE, PoCE, or ST between diabetic and nondiabetic patients treated with the Absorb BVS; 2) diabetic patients treated with the Absorb BVS showed 1-year rates of DoCE, PoCE, and ST similar to the matched diabetic patients treated with EES.

In general, diabetic patients undergoing PCI have an increased risk of restenosis and ST (10,19,20). Anatomic complexity of CAD, a phenotype expression of severity and duration of diabetic syndrome, may show a differential effect on the clinical outcomes in diabetic patients (21,22). In the present study, patient demographics and lesion characteristics were nearly identical between diabetic and nondiabetic patients treated with the BVS, and similar clinical outcomes were observed up to 1 year of follow-up. Specifically, the incidence rates of DoCE (3.7%) and definite/probable ST (0.7%) in diabetic patients treated with the BVS were favorable, although it should be emphasized that the present study included patients with relatively low risk profiles and noncomplex lesions. In addition, the potential underreporting of events related to the specific monitoring of the ABSORB EXTEND trial should be noted.

Current therapeutic guidelines recommend DES rather than BMS for diabetic patients undergoing PCI for obstructive CAD (23,24). These guidelines, however, rely on the data derived from first-generation DES, showing considerable risk reduction of restenosis and TLR compared with BMS (4). Conversely, first-generation DES raised safety concerns regarding an increased risk of very late ST (25–27). Five-year follow-up data of the LEADERS (Limus Eluted From A Durable Versus ERodable Stent Coating) trial indicated that the newer generation biolimus-eluting stent with biodegradable polymer was associated with significantly lower incidence of PoCE and very late ST compared with the first-generation sirolimus-eluting stent in

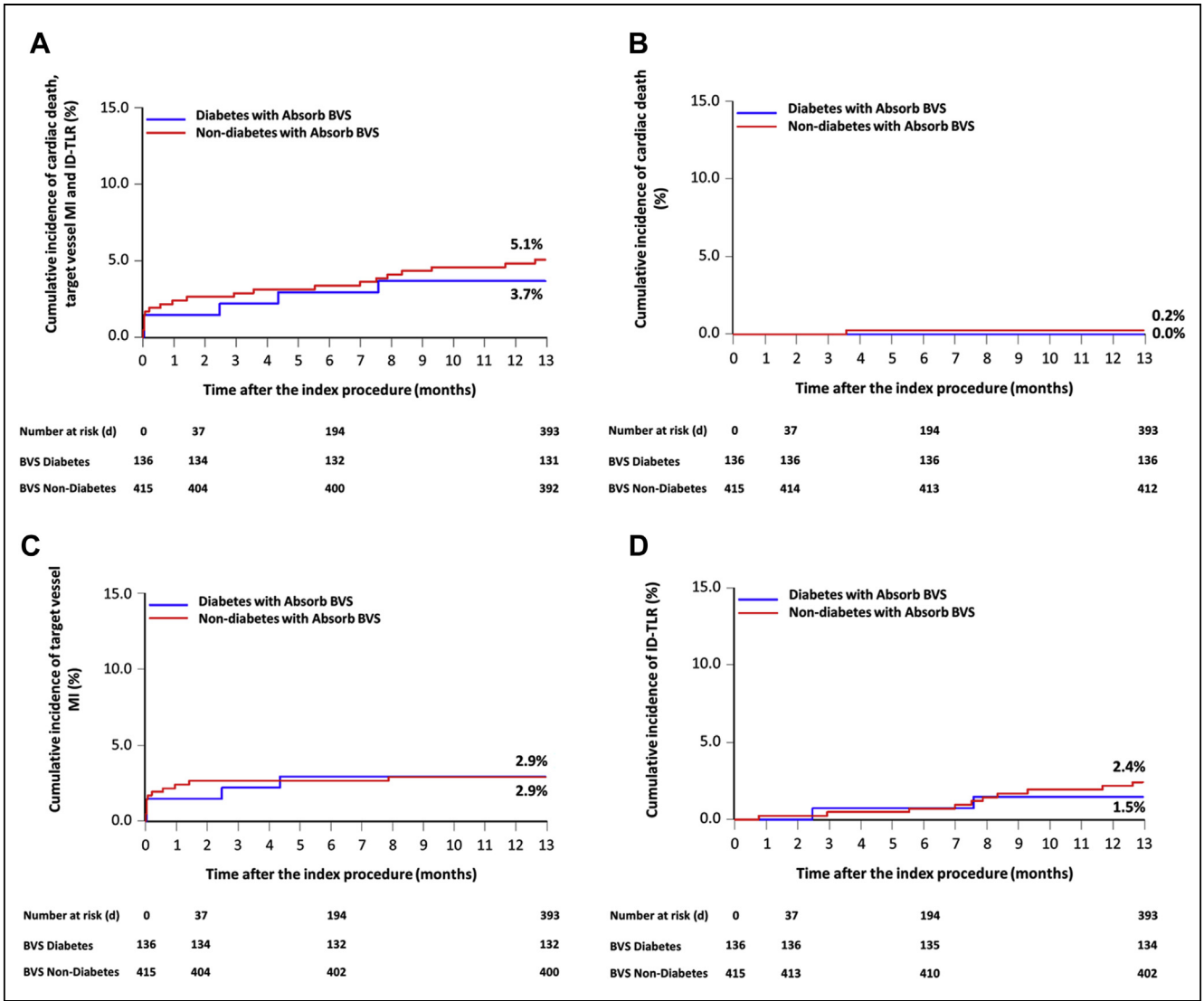

Figure 2. Time-to-Event Curves for DoCE and the Components in Diabetic and Nondiabetic Patients Treated With the ABSORB BVS Up to 1-Year Follow-Up

The cumulative incidences of adverse cardiac events are shown separately: DoCE **(A)**, cardiac death **(B)**, target-vessel MI **(C)**, and ID-TLR **(D)**. BVS = bioresorbable vascular scaffold; DoCE = device-oriented composite endpoint; ID-TLR = ischemia-driven target lesion revascularization; MI = myocardial infarction.

the entire study group (9). Although the ESSENCE-DIABETES (Randomized Comparison of Everolimus-Eluting Stent Versus Sirolimus-Eluting Stent Implantation for De Novo Coronary Artery Disease in Patients With Diabetes Mellitus) trial and the diabetic subgroup analysis of the RESET (Randomized Evaluation of Sirolimus-eluting Versus Everolimus-Eluting Stent) trial showed the favorable trends toward the EES compared with the sirolimus-eluting stent, no data have supported the superiority of newer generation DES over first-generation DES in diabetic patients with respect to clinical outcomes (28,29). In the present analysis, a large number of diabetic patients from the SPIRIT trials facilitated fair comparisons between 2 different technologies eluting the same antiproliferative drug everolimus by means of PS matching. One-year DoCE was observed in 3.9% and 6.4% in the BVS and EES groups, respectively ($p = 0.38$). Although this result should be interpreted with caution due to the limited sample size and post-hoc analysis nature, our data suggest that the Absorb BVS is feasible, safe, and effective for the treatment of diabetic patients with noncomplex lesions.

Insulin and insulin-like growth factors promote stimulatory action on vascular smooth muscle cells, which might result in accelerated smooth muscle cell proliferation after coronary stenting (30). Everolimus reduces excessive neointimal hyperplasia by inhibiting the mammalian target of rapamycin that subsequently interferes with cellular mitosis. This process is tightly regulated by glycosylation-dependent

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Table 2. Clinical Outcomes of Diabetic and Nondiabetic Patients Treated With the Absorb BVS at 1-Year Follow-Up

Outcomes	Absorb BVS: Diabetic Patients (N = 136)		Absorb BVS: Nondiabetic Patients (N = 415)		p Value
	% (n/N)	95% CI	% (n/N)	95% CI	
Device-oriented composite endpoint	3.7 (5/136)	1.2–8.4	5.1 (21/415)	3.2–7.6	0.64
Components (nonhierarchical)					
Cardiac death	0.0 (0/136)	0.0–2.7	0.2 (1/415)	0.0–1.3	1.00
Target vessel MI	2.9 (4/136)	0.8–7.4	2.9 (12/415)	1.5–5.0	1.00
Q-wave MI	0.0 (0/136)	0.0–2.7	1.0 (4/415)	0.3–2.5	0.58
Non–Q-wave MI	2.9 (4/136)	0.8–7.4	1.9 (8/415)	0.8–3.8	0.50
ID-TLR	1.5 (2/136)	0.2–5.2	2.4 (10/415)	1.2–4.4	0.74
CABG	0.0 (0/136)	0.0–2.7	0.2 (1/415)	0.0–1.3	1.00
PCI	1.5 (2/136)	0.2–5.2	2.2 (9/415)	1.0–4.1	1.00
Patient-oriented composite endpoint	7.4 (10/136)	3.6–13.1	8.2 (34/415)	5.7–1.3	0.86
Components (nonhierarchical)					
All-cause death	0.0 (0/136)	0.0–2.7	0.7 (3/415)	0.2–2.1	1.00
All MI	2.9 (4/136)	0.8–7.4	2.9 (12/415)	1.5–5.0	1.00
Q-wave MI	0.0 (0/136)	0.0–2.7	1.0 (4/415)	0.3–2.5	0.58
Non–Q-wave MI	2.9 (4/136)	0.8–7.4	1.9 (8/415)	0.8–3.8	0.50
Any repeat revascularization	5.1 (7/136)	2.1–10.3	5.1 (21/415)	3.2–7.6	1.00
CABG	0.0 (0/136)	0.0–2.7	0.7 (3/415)	0.2–2.1	1.00
PCI	5.1 (7/136)	2.1–10.3	4.6 (19/415)	2.8–7.1	0.82
Scaffold thrombosis per ARC definition					
Acute, <1 day					
Definite	0.0% (0/136)	0.0–2.7	0.0% (0/415)	0.0–0.9	NA
Probable	0.0% (0/136)	0.0–2.7	0.0% (0/415)	0.0–0.9	NA
Possible	0.0% (0/136)	0.0–2.7	0.0% (0/415)	0.0–0.9	NA
Definite + probable	0.0% (0/136)	0.0–2.7	0.0% (0/415)	0.0–0.9	NA
Subacute, 1–30 days					
Definite	0.0 (0/136)	0.0–2.7	0.2 (1/415)	0.0–1.3	1.00
Probable	0.0 (0/136)	0.0–2.7	0.2 (1/415)	0.0–1.3	1.00
Possible	0.0 (0/136)	0.0–2.7	0.0 (0/415)	0.0–0.9	NA
Definite + probable	0.0 (0/136)	0.0–2.7	0.5 (2/415)	0.1–1.7	1.00
Late, 31–365 days					
Definite	0.7 (1/136)	0.0–4.0	0.2 (1/414)	0.0–1.3	0.43
Probable	0.0 (0/136)	0.0–2.7	0.0 (0/414)	0.0–0.9	NA
Possible	0.0 (0/136)	0.0–2.7	0.2 (1/414)	0.0–1.3	1.00
Definite + probable	0.7 (1/136)	0.0–4.0	0.2 (1/414)	0.0–1.3	0.43
Overall up to 1 yr (0–365 days)					
Definite	0.7 (1/136)	0.0–4.0	0.5 (2/414)	0.1–1.7	0.57
Probable	0.0 (0/136)	0.0–2.7	0.2 (1/414)	0.0–1.3	1.00
Possible	0.0 (0/136)	0.0–2.7	0.2 (1/414)	0.0–1.3	1.00
Definite + probable	0.7 (1/136)	0.0–4.0	0.7 (3/414)	0.2–2.1	1.00

ARC = Academic Research Consortium; CABG = coronary artery bypass graft; CI = confidence interval; ID-TLR = ischemia-driven target lesion revascularization; MI = myocardial infarction; PCI = percutaneous coronary intervention; other abbreviations as in Table 1.

enzymes in contrast to paclitaxel, which interferes with multiple cellular processes (31). Indeed, a previous pooled analysis suggested an interaction between insulin use and drug type for the incidence of ischemia-driven TLR (10). In the present study, there were no significant differences in the incidence of DoCE among patients with insulin-treated diabetes, noninsulin-treated diabetes, and no diabetes treated with the BVS. In addition, 1-year rates of DoCE in insulin-treated diabetic patients were similar between the BVS and EES (8.7% vs. 8.8%, p = 1.0), although the present study might be underpowered to elicit small differences due to the sample size and relatively short follow-up period.

The ARC recommended 2 methodological approaches to report composite clinical outcomes: DoCE and PoCE. In

Table 3. Baseline Characteristics of Diabetic Patients Before and After Propensity-Score Matching

	Before PS Matching			After PS Matching		
	Absorb BVS Diabetes (n = 136)	EES Diabetes (n = 882)	p Value	Absorb BVS Diabetes (n = 102)	EES Diabetes (n = 172)	p Value
Demographic characteristics						
Age, yrs	61.6 ± 10.0 (136)	63.6 ± 9.9 (882)	0.032	62.2 ± 9.8 (102)	62.2 ± 9.7 (172)	0.97
Male sex	73.5 (100/136)	64.3 (567/882)	0.035	71.6 (73/102)	66.9 (115/172)	0.42
Current smoker	19.9 (27/136)	18.5 (159/859)	0.71	19.6 (20/102)	20.3 (35/172)	0.88
Hypertension requiring medication	75.0 (102/136)	85.6 (754/881)	0.002	84.3 (86/102)	80.2 (138/172)	0.40
Hypercholesterolemia requiring medication	67.6 (92/136)	82.3 (718/872)	<0.001	73.5 (75/102)	76.7 (132/172)	0.55
Diabetes treatment						
Insulin	16.9 (23/136)	25.7 (227/882)	0.025	18.6 (19/102)	20.9 (36/172)	0.76
Oral hypoglycemic drugs	74.3 (101/136)	59.8 (527/882)	0.001	73.5 (75/102)	65.7 (113/172)	0.23
Physical exercise and/or diet modification only	4.4 (6/136)	9.8 (86/882)	0.052	3.9 (4/102)	9.3 (16/172)	0.15
No treatment	4.4 (6/136)	4.8 (42/882)	1.00	3.9 (4/102)	4.1 (7/172)	1.00
Family history of coronary artery disease	41.4 (53/128)	51.1 (377/738)	0.043	45.1 (46/102)	48.8 (84/172)	0.55
Unstable angina	33.8 (46/136)	26.5 (229/864)	0.08	31.4 (32/102)	31.4 (54/172)	1.00
Previous coronary intervention	23.5 (32/136)	34.7 (305/880)	0.010	21.6 (22/102)	31.4 (54/172)	0.08
Previous myocardial infarction	26.5 (36/136)	22.0 (187/849)	0.25	25.5 (26/102)	26.2 (45/172)	0.90
No. of diseased vessels						
Multivessel disease	23.5 (32/136)	41.7 (368/882)	<0.001	25.5 (26/102)	22.7 (39/172)	0.60
Target vessel	144 lesions	1,035 lesions		108 lesions	183 lesions	
Right coronary artery	36.8 (53/144)	28.8 (298/1,035)	0.049	37.0 (40/108)	24.0 (44/183)	0.018
Left anterior descending artery	36.1 (52/144)	41.4 (429/1,035)	0.22	35.2 (38/108)	49.7 (91/183)	0.016
Left circumflex artery or ramus	27.1 (39/144)	29.7 (307/1,035)	0.52	27.8 (30/108)	26.2 (48/183)	0.77
Left main coronary artery	0.0 (0/144)	0.1 (1/1,035)	1.00	0.0 (0/108)	0.0 (0/183)	NA
ACC/AHA lesion class	143 lesions	1026 lesions		108 lesions	183 lesions	
A/B1	62.9 (90/143)	44.5 (457/1,026)	<0.001	60.2 (65/108)	55.2 (101/183)	0.41
B2/C	37.1 (53/143)	55.5 (569/1,026)	<0.001	39.8 (43/108)	44.8 (82/183)	0.41
Target lesion characteristics	144 lesions	1,035 lesions		108 lesions	183 lesions	
Lesion length, mm	11.7 ± 5.1 (143)	15.3 ± 6.6 (1,026)	<0.001	12.2 ± 5.2 (108)	12.6 ± 5.2 (183)	0.56
Pre-procedure						
Reference vessel diameter, mm	2.60 ± 0.33 (143)	2.74 ± 0.47 (1,029)	<0.001	2.62 ± 0.32 (108)	2.64 ± 0.41 (183)	0.62
Minimal luminal diameter, mm	1.07 ± 0.33 (144)	0.77 ± 0.39 (1,033)	<0.001	1.04 ± 0.30 (108)	0.99 ± 0.36 (183)	0.28
% diameter stenosis	58.8 ± 10.8 (144)	71.2 ± 12.6 (1,033)	<0.001	60.5 ± 9.5 (108)	62.4 ± 10.3 (183)	0.11
Dual antiplatelet therapy*						
At discharge	100.0 (136/136)	98.1 (862/879)	0.15	100.0 (102/102)	97.1 (167/172)	0.16
At 6 months	96.3 (131/136)	95.2 (837/879)	0.57	96.1 (98/102)	96.5 (166/172)	1.00
At 1 yr	82.4 (112/136)	81.2 (714/879)	0.75	83.3 (85/102)	79.7 (137/172)	0.45

Values are mean ± SD (N) and % (n/N).
EES = everolimus-eluting metal stent; PS = propensity score; other abbreviations as in Table 1.

the present analyses, we applied a DoCE as a primary endpoint because this represents the efficiency and efficacy of a new device. We also reported a PoCE because it represents the most critical clinical approach and may reflect the systemic risk and benefit for patients related to a new treatment. In the matched diabetic study group, the 1-year rate of PoCE was approximately twice as high as that of DoCE in both the BVS group and the EES group (3.9% for DoCE vs. 7.8% for PoCE in the BVS group and 6.4% for DoCE vs. 11.0% for PoCE in the EES group), driven by non–target lesion revascularizations. This finding is similar to those of previous DES studies (32) and highlights the importance of optimal medical therapies and life-style modification for glycemic control as well as the frequently accompanying comorbidities such as hypertension, dyslipidemia, and obesity if clinical outcomes of diabetic patients with obstrtrun -1uctive CAD are to be improved (33).

In the most recent report on serial angiographic assessment from the ABSORB Cohort B trial, the in-scaffold late loss of the BVS increased between 6 months and 1 year, whereas it remained stable after 1 year (0.16, 0.27, 0.27, and 0.29 mm at 6 months, 1 year, 2 years, and 3 years, respectively) (12,13,34). Conversely, in the SPIRIT II trial, the in-stent late loss of EES increased from 0.17 mm at

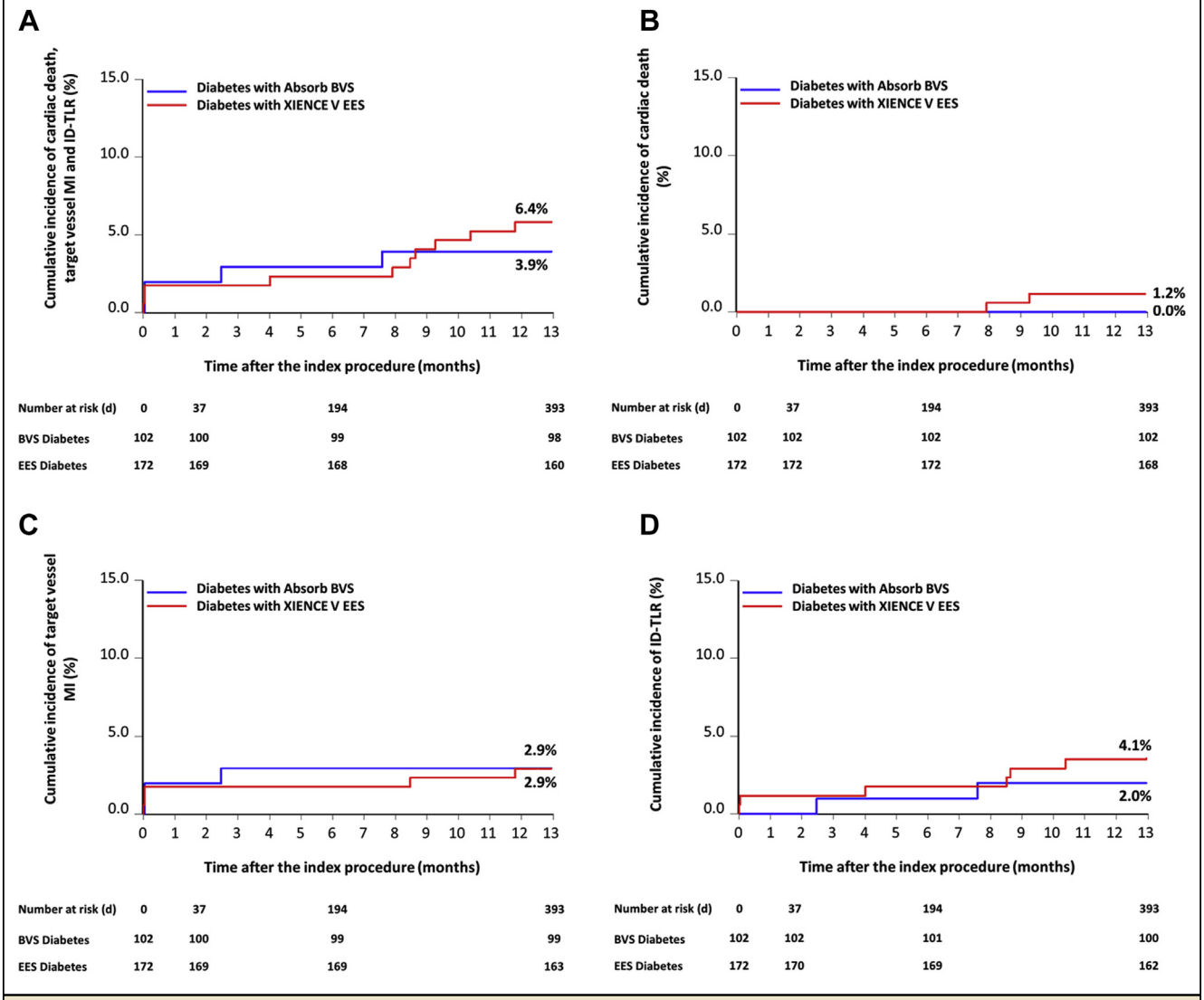

Figure 3. Time-to-Event Curves for DoCE and the Components in the Matched Diabetic Patients Treated With the BVS and in Those Treated With EES Up to 1-Year Follow-up

The cumulative incidences of adverse cardiac events are shown separately: DoCE **(A)**, cardiac death **(B)**, target-vessel MI **(C)**, and ID-TLR **(D)**. Abbreviations as in Figures 1 and 2.

6 months to 0.33 mm at 2 years (35). In this indirect comparison, the absolute change in late loss between 6 months and 2 years tended to be smaller with the BVS (Δ0.11 mm) than EES (Δ0.16 mm). More interestingly, intravascular ultrasound data demonstrated that the EES lumen volume slightly decreased between 6 months and 2 years in the SPIRIT II trial (159 mm^3 at 6 months and 153 mm^3 at 2 years), whereas the BVS mean lumen area significantly increased from 1 to 3 years (6.35 mm^2 at 1 year and 6.81 mm^2 at 3 years, $p < 0.001$) in the serial observation of the ABSORB Cohort B trial (12). This phenomenon can be explained by the fact that mean and minimal scaffold areas significantly increased and thereby compensated for neointimal hyperplasia. Therefore, the favorable trend toward BVS observed in 1-year clinical outcomes in the present study might become more pronounced with longer follow-up.

From a physiological perspective, the absence of permanent vessel caging facilitates the restoration of vasomotor function, adaptive shear stress, cyclic strain, and late luminal enlargement (11,36). In addition, fewer material triggers for very late ST such as uncovered struts and durable polymers would theoretically be present after bioresorption with the BVS compared with the DES (37). These beneficial effects

Table 4. Clinical Outcomes of Diabetic Patients Treated With BVS and EES at 1-Year Follow-Up

	Entire Population					Matched Population				
	Absorb BVS Diabetes (N = 136)		EES Diabetes (N = 882)			Absorb BVS Diabetes (N = 102)		EES Diabetes (N = 172)		
Outcomes	% (n/N)	95% CI	% (n/N)	95% CI	p Value	% (n/N)	95% CI	% (n/N)	95% CI	p Value
Device-oriented composite endpoint	3.7 (5/136)	1.2–8.4	6.3 (56/882)	4.9–8.3	0.22	3.9 (4/102)	1.1–9.7	6.4 (11/172)	3.2–11.2	0.38
Components (nonhierarchical)										
Cardiac death	0.0 (0/136)	0.0–2.7	1.0 (9/882)	0.5–1.9	0.62	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
Target vessel MI	2.9 (4/136)	0.8–7.4	2.7 (24/882)	1.8–4.0	0.78	2.9 (3/102)	0.6–8.4	2.9 (5/172)	1.0–6.7	1.00
Q-wave MI	0.0 (0/136)	0.0–2.7	0.2 (2/882)	0.0–0.8	1.00	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
Non–Q-wave MI	2.9 (4/136)	0.8–7.4	2.5 (22/882)	1.6–3.8	0.77	2.9 (3/102)	0.6–8.4	1.7 (3/172)	0.4–5.0	0.67
ID-TLR	1.5 (2/136)	0.2–5.2	3.9 (34/882)	2.7–5.4	0.21	2.0 (2/102)	0.2–6.9	4.1 (7/172)	1.7–8.2	0.49
CABG	0.0 (0/136)	0.0–2.7	0.7 (6/882)	0.3–1.5	1.00	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
PCI	1.5 (2/136)	0.2–5.2	3.3 (29/882)	2.2–4.7	0.42	2.0 (2/102)	0.2–6.9	3.5 (6/172)	1.3–7.4	0.71
Patient-oriented composite endpoint	7.4 (10/136)	3.6–13.1	12.4 (109/882)	10.3–14.7	0.09	7.8 (8/102)	3.5–14.9	11.0 (19/172)	6.8–16.7	0.39
Components (nonhierarchical)										
All-cause death	0.0 (0/136)	0.0–2.7	1.8 (16/882)	1.0–2.9	0.15	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
All MI	2.9 (4/136)	0.8–7.4	2.8 (25/882)	1.8–4.2	1.00	2.9 (3/102)	0.6–8.4	2.9 (5/172)	1.0–6.7	1.00
Q-wave MI	0.0 (0/136)	0.0–2.7	0.2 (2/882)	0.0–0.8	1.00	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
Non–Q-wave MI	2.9 (4/136)	0.8–7.4	2.6 (23/882)	1.7–3.9	0.77	2.9 (3/102)	0.6–8.4	1.7 (3/172)	0.4–5.0	0.67
Any repeat revascularization	5.1 (7/136)	2.1–10.3	9.3 (82/882)	7.5–11.4	0.11	5.9 (6/102)	2.2–12.4	9.3 (16/172)	5.4–14.7	0.31
CABG	0.0 (0/136)	0.0–2.7	1.8 (16/882)	1.0–2.9	0.15	0.0 (0/102)	0.0–3.6	2.9 (5/172)	1.0–6.7	0.16
PCI	5.1 (7/136)	2.1–10.3	7.7 (68/882)	6.0–9.7	0.29	5.9 (6/102)	2.2–12.4	7.0 (12/172)	3.7–11.9	0.72
SST per ARC definition										
Acute, <1 day										
Definite	0.0 (0/136)	0.0–2.7	0.2 (2/882)	0.0–0.8	1.00	0.0 (0/102)	0.0–3.6	0.6 (1/172)	0.0–3.2	1.00
Probable	0.0 (0/136)	0.0–2.7	0.0 (0/882)	0.0–0.4	NA	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Possible	0.0 (0/136)	0.0–2.7	0.0 (0/882)	0.0–0.4	NA	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Definite + probable	0.0 (0/136)	0.0–2.7	0.2 (2/882)	0.0–0.8	1.00	0.0 (0/102)	0.0–3.6	0.6 (1/172)	0.0–3.2	1.00
Subacute, 1–30 days										
Definite	0.0 (0/136)	0.0–2.7	0.1 (1/882)	0.0–0.6	1.00	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Probable	0.0 (0/136)	0.0–2.7	0.0 (0/882)	0.0–0.4	NA	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Possible	0.0 (0/136)	0.0–2.7	0.0 (0/882)	0.0–0.4	NA	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Definite + probable	0.0 (0/136)	0.0–2.7	0.1 (1/882)	0.0–0.6	1.00	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Late, 31–365 days										
Definite	0.7 (1/136)	0.0–4.0	0.5 (4/874)	0.1–1.2	0.52	1.0 (1/102)	0.0–5.3	1.2 (2/172)	0.1–4.1	1.00
Probable	0.0 (0/136)	0.0–2.7	0.2 (2/874)	0.0–0.8	1.00	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Possible	0.0 (0/136)	0.0–2.7	0.7 (6/874)	0.3–1.5	1.00	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
Definite + probable	0.7 (1/136)	0.0–4.0	0.7 (6/874)	0.3–1.5	1.00	1.0 (1/102)	0.0–5.3	1.2 (2/172)	0.1–4.1	1.00
Overall up to 1 yr (0–365 days)										
Definite	0.7 (1/136)	0.0–4.0	0.8 (7/874)	0.3–1.6	1.00	1.0 (1/102)	0.0–5.3	1.7 (3/172)	0.4–5.0	1.00
Probable	0.0 (0/136)	0.0–2.7	0.2 (2/874)	0.0–0.8	1.00	0.0 (0/102)	0.0–3.6	0.0 (0/172)	0.0–2.1	NA
Possible	0.0 (0/136)	0.0–2.7	0.7 (6/874)	0.3–1.5	1.00	0.0 (0/102)	0.0–3.6	1.2 (2/172)	0.1–4.1	0.53
Definite + probable	0.7 (1/136)	0.0–4.0	1.0 (9/874)	0.5–2.0	1.00	1.0 (1/102)	0.0–5.3	1.7 (3/172)	0.4–5.0	1.00

ST = scaffold/stent thrombosis; other abbreviations as in Tables 1 to 3.

of the BVS, however, are not expected to be evident until after 1 year. Therefore, longer clinical follow-up is needed to elucidate the differential consequences of the Absorb BVS from a permanent metal prosthesis, in particular, for the diabetic patients.

Study limitations. First, the present analysis included noncomplex lesions according to pre-specified trial protocols. Therefore, the clinical performance of the BVS in diabetic patients with complex lesions (e.g., diffuse lesion and calcified lesion) is still unknown. Second, despite the PS matching to allow fair comparisons between the BVS and the EES, the possibility of results being affected by unknown confounding factors cannot be excluded. Third, our results should be considered hypothesis generating due to the

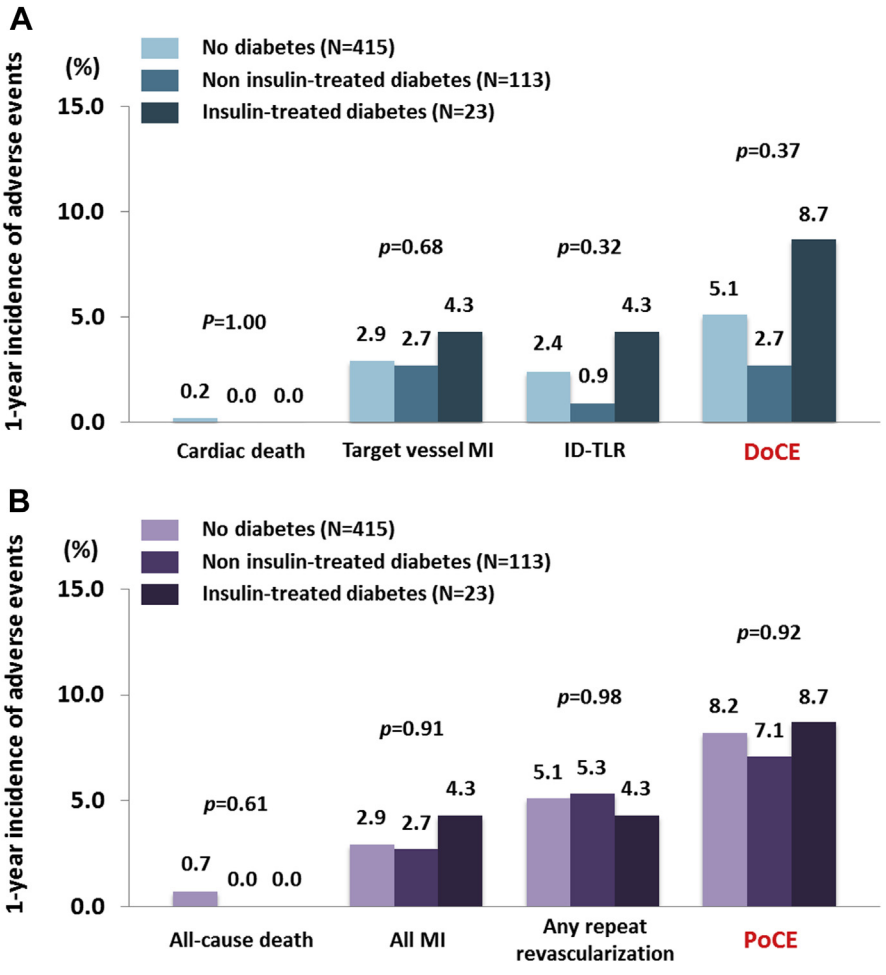

Figure 4. 1-Year Rates of Adverse Cardiac Events According to Diabetes Status in Patients Treated With the Absorb BVS

The 1-year rates of DoCE and the components **(A)** and those of PoCE and the components **(B)**. PoCE = patient-oriented composite endpoint; other abbreviations as in Figure 2.

nonrandomized, post-hoc nature of the analyses. In addition, the present analyses might be underpowered to demonstrate the differences of clinical efficacy between the devices. Further investigation is thus required in large-scale, randomized, controlled trials for a pre-specified diabetic study group.

Conclusions

In this first report of the Absorb BVS in diabetic patients, the 1-year incidence rate of DoCE was 3.7%, similar to that in nondiabetic patients. In addition, no differences in the rates of 1-year DoCE, PoCE, or ST were observed in diabetic patients treated with the Absorb BVS and the XIENCE V EES in the matched study group from pooled prospective trials. These promising results should stimulate future trials of the Absorb BVS in larger cohorts of diabetic patients with both complex and noncomplex lesions with long-term follow-up to demonstrate whether clinical advantages are present with this novel technology.

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Key Words: bioresorbable scaffold ■ coronary artery disease ■ diabetes mellitus ■ drug-eluting stent.

APPENDIX

For supplemental material including a table, please see the online version of this article.